Detection of 14-3-3 brain protein in cerebrospinal fluid of HIV infected patients

EDITOR,—The 14-3-3 proteins are a group of highly conserved proteins involved in intracellular signalling. Detection of 14-3-3 brain protein has been described in cerebrospinal fluid (CSF) of patients with transmissible spongiform encephalopathies including both sporadic and variant Creutzfeldt–Jakob disease.[1 2] False positive results have been reported in conditions producing (sub)acute neuronal destruction, including herpes simplex encephalitis, ischaemic stroke, multi-infarct dementia, and paraneoplastic syndromes.[1–3] We postulated that 14-3-3 brain protein may be detected in CSF from patients with HIV associated dementia complex (HADC) as this condition is characterised neuropathologically by a giant cell encephalitis, leucoencephalopathy, astrogliosis and neuronal loss.

We prospectively studied 17 HIV antibody positive patients (14 men) aged 27–60 (median 37) years, with CD4 counts of 0–220 (median 20) cells $\times 10^6$/l, who underwent lumbar puncture for investigation of HADC (six patients), staging of lymphoma (five patients), or investigation of other conditions (six patients): epilepsy (two), cervical radiculopathy (one), chronic demyelinating polyradiculopathy (one), CMV encephalitis (one), self limiting headache (one). Of those with HADC, the severity of dementia assessed using Memorial Sloan-Kettering criteria,[4] was mild in two and moderate in four. The degree of atrophy on cranial magnetic resonance imaging, used as a marker of neuronal loss[5] was mild in four and moderate in two. Clinical details of those with lymphoma are given in table 1. At each lumbar puncture an aliquot of CSF (250 µl) was frozen immediately at −20°C and stored for subsequent 14-3-3 protein analysis.

CSF was routinely processed as described previously.[6] Detection of 14-3-3 protein was done without knowledge of the patient's diagnosis, using a technique described by Hsich *et al*,[1] modified to use anti-14-3-3 γ polyclonal rabbit antibody.

In 14 of 17 patients CSF was negative for 14-3-3 protein. Of the three with detectable 14-3-3 protein in CSF, all had lymphoma but only one had CNS disease, the other two had only extraneural disease (table 1). These data, although from a small study population, suggest that detection of 14-3-3 protein in CSF is not useful for diagnosis of HADC. Detectable 14-3-3 protein has previously been reported in a non-HIV infected patient with CNS lymphoma,[3] so this observation in our patient is not unique, although brain necrosis from coexisting cerebral toxoplasmosis provides an alternative explanation. Of the two patients with extraneural lymphoma and detectable 14-3-3 protein in CSF, one had EBV DNA in CSF and so was at high risk of developing cerebral lymphoma. This possibility could not be confirmed as necropsy was not performed. In neither of the latter two patients was there a CSF pleocytosis, so contamination by 14-3-3 protein derived from peripheral blood leucocytes is unlikely. In the final case the absence of limbic encephalitis or cerebellar degeneration[3] makes it difficult to ascribe the finding to a paraneoplastic process.

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1 Hsich G, Kenney K, Gibbs C J, *et al*. The 14-3-3 brain protein in cerebrospinal fluid as a marker for transmissible spongiform encephalopathies. *N Engl J Med* 1996;**335**:924–30
2 Zeidler M, Stewart GE, Barraclough CR, *et al*. New variant Creutzfeldt-Jakob disease: neurological features and diagnostic tests. *Lancet* 1997;**350**:903–7
3 Saiz A, Graus F, Dalmau J, *et al*. Detection of 14-3-3 brain protein in the cerebrospinal fluid of patients with paraneoplastic neurological disorders. *Ann Neurol* 1999;**46**: 774–7.
4 Price RW, Brew BJ. The AIDS dementia complex. *J Infect Dis* 1988;**158**:1079–83.
5 Miller RF, Lucas SB, Hall-Craggs MA, *et al*. Comparison of magnetic resonance imaging with neuropathological findings in the diagnosis of HIV and CMV associated CNS disease in AIDS. *J Neurol Neurosurg Psychiatry* 1997;**62**: 346–51.
6 Miller RF, Hall-Craggs MA, Costa DC, *et al*. Magnetic resonance imaging, thallium-201 SPET scanning and laboratory analyses for discrimination of cerebral lymphoma and toxoplasmosis in AIDS. *Sex Transm Inf* 1998;**74**: 258–64.

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Hepatitis B vaccination in a high risk MSM population: the need for vaccine education

EDITOR,—Estimates of the prevalence of hepatitis B virus (HBV) markers among men who have sex with men (MSM) range from 5% to 81%, and the prevalence of HBV surface antigen varies from 1% to 11%.[1 2] Despite a safe and effective vaccine against HBV, sexually active MSM are not vaccinated adequately.[2–5] Few empirical data describe the factors associated with HBV vaccination among MSM. We conducted a study to identify correlates of HBV vaccination among MSM that could inform future interventions designed to enhance HBV vaccination.

Data were collected at two male "gay" bars in Birmingham, Alabama, USA, using a brief, self administered questionnaire. Of 130 bar patrons, our sample consisted of 111 respondents who identified themselves as MSM and knew their vaccination status. Their average age was 31 years with a range of 18–48 years. The sample was disproportionately white (91.9%); 42% reported being vaccinated for HBV.

Based on bivariate associations nine characteristics were significantly associated with HBV vaccination—age; condom use; factual knowledge of hepatitis; HBV knowledge; HCV knowledge; HBV vaccination knowledge; number of sources for information about hepatitis; information from a physician; and information from professional training. Two factors retained significance when adjusting for all other factors in a multivariate logistic regression model: respondents' HBV vaccination knowledge (OR=10.18; 90% CI = 4.0–25.37, p = 0.0001) and their frequency of condom use (OR=6.1; 90% CI = 2.54–14.67, p = 0.0007). The predictive power of the model ($\chi^2 = 42.33$; p = 0.0001) was high, correctly classifying 76.4% of the respondents into their actual vaccination status categories (p = 0.0001). These findings suggest that respondents with high HBV vaccination knowledge and condom use are significantly more likely to have been vaccinated against HBV.

There is need to enhance awareness and facilitate vaccination among this high risk population for HBV infection; 32% reported having no information about hepatitis. Many respondents reported engaging in behaviours that put them and their sexual partners at risk for HBV infection; 95.5% and 30.6% reported using a condom less than 50% of the

Table 1 Clinical features, results of CSF brain protein detection, and outcome in patients with lymphoma

			CSF		
Patient	*Type of lymphoma*	*No of lumbar puncture*	*Interval between lumbar puncture (weeks)*	*14-3-3 detection*	*Outcome*
1	Primary CNS	1		No	Died 2 weeks after second lumbar puncture
			11		Necropsy showed also cerebral toxoplasmosis
		2		Yes	
2	Primary CNS	1		No	Died 2 weeks after second lumbar puncture
			3		Necropsy confirmed diagnosis
		2		No	
3	Primary CNS	1	NA	No	Died 3 weeks later. No necropsy
4	Systemic, disseminated extraneural	1	NA	Yes	Died 6 weeks later. Cranial MR scan normal but EBV DNA detected in cell free CSF No necropsy
5	Systemic, extra neural	1	NA	Yes	Alive. Cranial MR scan normal. Treated with local RT and HAART. No lymphoma recurrence after 39 months follow up

CNS = central nervous system. NA = not applicable. EBV = Epstein–Barr virus. CSF = cerebrospinal fluid. MR = magnetic resonance. RT = radiotherapy. HAART = highly active antiretroviral therapy.